ENVIRONMENTAL PROTECTION AGENCY

EPA Office of Science and Coordination Policy: *Laboratory Support for In Vitro Assays and Physical Chemical Property Tests* (Task Order, 03)

Request for Task Order Proposal (RFTOP) Revised

68HERH19Q0082

EPA Office of Science and Coordination Policy: *Laboratory Support for In Vitro Assays and Physical Chemical Property Tests*

1 PERFORMANCE WORK STATEMENT (PWS)

1.1 PURPOSE

The purpose of this task order (TO), *EPA Office of Science and Coordination Policy:* ***Laboratory Support for In Vitro Assays and Physical Chemical Property Tests****,* is to obtain laboratory support for the Office of Science Coordination and Policy (OSCP), Office of Chemical Safety & Pollution Prevention (OCSPP) in two (2) general areas:

1. In vitro assays that support In-vitro to In-vivo Extrapolations (IVIVE)
2. Tests to determine physical chemical properties of select chemicals

1.2 BACKGROUND

The Office of Science and Coordination Policy (OSCP) manages EPA's Endocrine Disruptor Screening Program (EDSP) and two federal advisory committees, FIFRA Scientific Advisory Panel and the TSCA Scientific Advisory Committee on Chemicals.

The Endocrine Disruptor Screening Program (EDSP) was established in 1998 under authorities contained in the 1996 Food Quality Protection Act (FQPA) and the 1996 Safe Drinking Water Act (SDWA) amendments. As mandated by these statutes, the EDSP develops a screening program to determine whether certain substances may have endocrine activity in humans and wildlife. The US EPA has developed a two-tiered approach for screening chemicals and pesticides. The Tier 1 battery is used to identify substances that have potential to interact with the estrogen, androgen or thyroid hormone pathways. The Tier 2 tests identify and establish dose response information for adverse effects for substances identified in the Tier 1 screening. Beginning in 2015, the EDSP is incorporating ToxCast high throughput screening data and computational models in the prioritization and screening of a chemical's potential to interact with the endocrine system in humans and wildlife for a portion of the Tier 1 battery. This approach will allow nearly 20 times the current number of screenings to be performed while nearly eliminating animal testing, allowing the program to meet its goals with a relatively level budget.

The EPA's EDSP is continuing the development and validation of alternative testing methodologies (i.e., high throughput assays and computational tools) to prioritize and screen chemicals based on potential endocrine bioactivity and exposure--in particular, the estrogen, androgen, or thyroid hormone pathways in humans and wildlife. This increased use of alternative testing methodologies will improve the output of screening results, allowing for greater coverage of the endocrine system.

1.3 TASK 1: TASK ORDER MANAGEMENT AND REPORTING REQUIREMENTS

1.3.1 The Contractor shall schedule a kick-off meeting/conference call with the TOCOR within 10 business days following the TO award. The TOCOR, Alternate (Alt) TOCOR, contract-level COR, and the EPA Contracting Officer (CO) must be invited to the kick-off meeting. Additional participants may be included.

~~1.3.2~~ The Contractor shall manage all aspects of the task order including, but not limited to, the technical, quality assurance, schedule, cost, and communication requirements.

1.3.3 The Contractor shall only work on tasks in the Performance Work Statement as directed by the TOCOR. The TOCOR shall identify specific due dates for deliverables for Tasks 3 and 4 via technical direction. Technical direction will be provided in writing by the Contracting Officer or the TOCOR as delegated by the Contracting Officer.

1.3.4 The Contractor shall schedule at least biweekly meetings (teleconference, in-person, Skype, Adobe Connect, or other media) with the TOCOR to discuss the status of the work including reporting any issues with respect to schedule slip or cost overruns. The TOCOR will identify, as needed, other individuals who should participate in these calls. Additional teleconference calls may be scheduled by the TOCOR as needed. Note: Telephone or in-person reports are not replacements for required written communications.

1.3.5 In addition to biweekly meeting, the Contractor shall update the TOCOR via telephone (and follow-up via e-mail) and, in writing, via e-mail, of any issues on an ongoing basis.

1.3.6 The Contractor shall immediately inform the TOCOR when any hours or costs for any task has exceeded or is expected to exceed the contractor estimate by >10%.

1.3.7 The Contractor shall immediately inform the TOCOR of any problems that may impact the production, budget, and/or delivery of deliverables.

1.3.8 The Contractor shall notify the TOCOR when 75% of the Government approved hours or approved LH (labor hour) costs have been incurred (including unbilled hours and costs).

1.3.9 The Contractor shall provide a monthly progress report of the combined monthly technical and financial progress report) stating the progress made, including the percentage of the project completed, a description of the work accomplished to support the cost, the estimated percentage of task completed (including deliverables) during the reporting period. The **Executive Summary shall summarize the planned and actual work for the month, financial status, work planned for the next month, and significant issues, risks, or concerns. The monthly report shall also provide cost and technical progress data for each of the six (6) defined tasks (by labor category for each task) and projected costs for the upcoming reporting period.**

1.3.10 **For the technical progress report also include the following specific information:**

- Narrative detail review of accomplishments during the reporting period and/or significant events, as well as an assessment of work being completed on schedule and budget.
- Status of all ongoing activities in accordance with the technical proposal and technical directives.
- List of deliverables with delivery dates (planned versus actual).
- Anticipated activities and deliverables for the next reporting period.
- Specific discussions shall include difficulties encountered and remedial action taken during the reporting period, and anticipated activity with a schedule of deliverables for the subsequent reporting period.

- List of current contractors / staffing roster and any changes that may impact deliverables in advance of the reporting period (e.g., change in personnel and vacations).
- Monthly Contractor performance information (performance metrics)

1.3.11 **For the financial report, include the following information:**

- Identification of cost issues or concerns
- For the current period, display the amount claimed.
- For the cumulative period display the total amount claimed; amount paid; amount suspended or disallowed; and remaining amount.
- Labor hours.

  (i) A list of employees, their labor categories, and the number of hours worked for the reporting period.
  (ii) For the current reporting period display the expended direct labor hours (by EPA contract labor category), and the total loaded direct labor hours.
  (iii) For the cumulative reporting period and the cumulative contract period display: The negotiated and expended direct labor hours (by EPA labor hour category) and the loaded direct labor rate.
  (iv) Display the estimated direct labor hours and costs to be expended during the next reporting period.
  (v) Display the estimates of remaining direct labor hours and costs required to complete the task order
- Unbilled allowable costs. Display the total costs incurred but unbilled for the current reporting period and cumulative for the task order.
- Average total cost labor hour. For the current contract period, compare the actual total cost per hour to date with the average total cost per hour of the approved technical proposal for the task order.
- The monthly report does not change the notification requirements of the "Limitation of Cost" or "Limitation of Funds" clauses requiring separate written notice to the Contracting Officer.

1.3.12 The Contractor shall maintain a cumulative record of all communications between the contractor and EPA (all media including e-mail and telephone calls) and provide it to the TOCOR within one month after the TO has ended.

1.3.13 The contractor shall provide all deliverables in an electronic format specified by the EPA TOCOR (e.g., Word, Excel, Access, HTML) via electronic mail. The Contractor shall format any deliverables intended for posting on an EPA public website to comply with Section 508.

1.3.14 Unless otherwise specified by the TOCOR, the Contractor shall provide a secure method for internet transfer of large files.

1.3.15 All deliverables for this task order are the property of EPA.

1.3.16 Contractor personnel shall identify themselves as contractor employees and shall not present themselves as EPA employees. Furthermore, they shall not represent view of the U.S. Government, EPA, or its employees. In addition, the contractor shall not engage in inherently governmental activities, including, but not limited to actual determination of EPA policy and preparation of documents on EPA letterhead other than routine correspondences.

1.4 TASK 2. QUALITY ASSURANCE AND QUALITY ASSURANCE PROJECT PLAN (QAPP)

The Contractor shall implement a quality system that meets ANSI standard E4-2014.

For planning purposes, assume that a Quality Assurance Project Plan (QAPP) will be required for Tasks 3 and 4). The contractor shall create a Quality Assurance Project Plan (QAPP) that documents the planning, implementation, and assessment procedures for quality assurance and quality control activities. The QAPP integrates all the technical and quality aspects of the project to provide a blueprint for obtaining the type and quality of environmental data and information needed for a specific decision or use. The QAPP shall be prepared in accordance with the specifications identified by EPA (found at https://www.epa.gov/quality/epa-qar-5- epa-requirements-quality-assurance-project-plans).

- Within 10 business days after Task Order Award, the contractor shall prepare and submit for EPA review a draft Quality Assurance Project Plan (QAPP) for Task 3 and Optional Task 4.
- EPA will review the contractor's draft QAPP and provide the Contractor with written approval or written comments.
- If needed, the Contractor shall submit a revised QAPP within 5 business days of receipt of the written comments on the draft QAPP, unless otherwise instructed by the EPA TO COR.
- Under no circumstances shall work that involves the generation, collection, evaluation, analysis, or use of environmental data be performed by the contractor until the contractor receives written notification from the EPA TO COR that EPA has approved the contractor's QAPP.
- All QA documentation, including the QAPP, prepared under this Task Order, shall be considered non-proprietary, and shall be made available to the public upon request.
- The contractor also shall provide EPA with monthly reports of QA-related activities performed during implementation of this Task Order. These monthly QA reports shall identify QA activities performed to support implementation of this task order, problems encountered, deviations from the QAPP, and corrective actions taken.

1.5 TASK 3: *IN VITRO* MEASUREMENTS FOR TOXICOKINETICS

Purpose: The purpose of Task 3 is to obtain laboratory services and support to perform specific *in vitro* assays which will be incorporated into toxicokinetic models (e.g. PBTK models) to predict internal tissue (plasma/blood) concentrations from the bioactivity concentrations determined using high throughput screening (HTS) *in vitro* assay data. EPA is working on methods related to extrapolate in vitro effects to in vivo responses, i.e., in vitro to in vivo extrapolation (IVIVE). Key species-specific parameters of IVIVE models that successfully generate predictions of in vivo doses from effective in vitro concentration include the collection of in vitro plasma protein binding and intrinsic hepatic metabolic clearance data. In vitro toxicokinetics, plasma protein binding and metabolic clearance, data will be collected using trout, rat, and human plasma and hepatocytes, respectively. Chemical-specific analytic methods are also needed to quantify the presence of compounds in the assay samples to determine plasma protein binding and intrinsic hepatic metabolism clearance rates.

Task 3.1.: Generate Standard Operating Procedures (SOPs)

****Task 3.1 will be Firm Fixed Price (FFP)

The contractor must generate Standard Operating Procedures (SOPs) for the following *in vitro* assays for three species (human, rat, and rainbow trout) and analytical chemistry methods:

In vitro Assays in human, rat, and rainbow trout:

- Plasma protein binding assay; and

- Hepatic metabolic clearance assay.

Analytical Chemistry Methods:
- Gas chromatography with mass spectrometric (GC/MS) detection or tandem mass spectrometric (GC-MS/MS) chemical analysis;
- High (or Ultra high) performance liquid chromatography with mass spectrometric (LC/MS) detection or tandem mass spectrometric (LC-MS/MS) chemical analysis;
- High performance liquid chromatography with fluorescence (HPLC/FLD) detection, ultra-violet/visible (HPLC/UV-VIS) chemical analysis.

A. Plasma Protein Binding Assays

All plasma sources must be approved by the TO COR. The SOPs for the following plasma protein binding assays should incorporate the following items:
- Total protein measurement shall be conducted, along with albumin and α-acyl-glycoprotein (AAG) quantification, on each plasma lot;
- All laboratory supplies that contact the test chemical, when possible, will be glass and if glass is not feasible or impossible then polypropylene is recommended;
- Plasma pH should be adjusted to normal physiological levels (i.e., 7.4) before use, if needed;
- Chemical solutions for dosing (either in buffer or solvent) should be incubated to be at the testing temperature prior to use;
- Solvent or spiking concentrations need to be kept to a minimum (≤0.5% v/v or lower) with substrate concentrations below aqueous solubility;
- Controls will include: An equilibrium control (chemical + buffer with dialysis but no plasma) to ensure equilibrium is achieved, and; a stability control (chemical + plasma without dialysis) to determine loss due to plasma degradation/metabolism;

i. Human Plasma Protein Binding Assay

A human plasma protein binding assay will be developed using the Rapid Equilibrium Dialysis (RED) method with possible modifications (e.g., Wetmore *et al.* 2012; Wetmore *et al.* 2013). Human plasma shall be a source pooled across multiple adult donors ($n \geq 6$) of mixed gender less than 65 years of age. Human plasma will be obtained from a documented commercial source, in compliance with any and all federal regulations and shall be similar or equivalent to the sources used in Rotroff *et al.* (2010) and Wetmore *et al.* (2012). Other references are available in Appendix A.

ii. Rat Plasma Protein Binding Assay

A rat plasma protein binding assay will be developed using the RED method with possible modifications (e.g., Wetmore *et al.* 2012; Wetmore *et al.* 2013). Rat plasma shall be a source pooled across multiple adult donors ($n \geq 6$) of mixed gender. Rat plasma will be obtained from a documented commercial source, in compliance with any and all federal regulations and shall be similar or equivalent to the source used in Wetmore *et al.* (2013). Other references are available in Appendix A.

iii. Rainbow Trout Plasma Protein Binding Assay

A rainbow trout plasma protein binding assay will be developed using the RED method with possible modifications (e.g., Wetmore *et al.* 2012; Wetmore *et al.* 2013). Rainbow trout plasma will ideally be a source pooled across multiple sexually immature animals ($n \geq 6$) of mixed gender. Rainbow trout plasma will be obtained from a documented source, in compliance with any and all federal regulations and, if possible, a commercial source should be used. Special care should be taken to ensure that the trout used are not treated with hormones. For this task, along with the citations listed in Appendix A, Escher *et al.* (2011) should also be referenced.

B. Metabolic Clearance Assays

Metabolic clearance assays, regardless of species, shall follow the Basic Protocol 4 as outlined in Fay *et al.* (2015) in terms of laboratory equipment and general protocol. Hepatocyte handling procedures, including temperatures, shall be species specific. All hepatocyte sources must be approved by the TO COR.
The SOPs for the following metabolic clearance assays should incorporate the following items:

- Each cell lot shall be analyzed for five Phase I and Phase II enzyme activity assays (EROD, ECOD, UGT, SULT, & GST) to demonstrate metabolic capacity;
- All laboratory supplies that contact the test chemical, when possible, will be glass and if glass is not feasible or impossible then polypropylene is recommended;
- Viability shall also be assessed for each cell lot and shall be 85% or greater to be used;
- Chemical solutions for dosing (either in buffer or solvent) should be incubated long enough to be at the testing temperature prior to use;
- Concentrations of solvent need to be kept to a minimum (≤0.5% v/v or lower) with substrate concentrations below aqueous solubility;
- Negative control shall consist of metabolically inactivated hepatocytes. It is recommended that metabolically inactivated hepatocytes are generated using a rigorous multiple (> 2x) freeze/thaw procedure. The method of generating metabolically inactivated hepatocytes shall be validated through measurement of Phase I and Phase II enzyme activity assays (EROD, ECOD, UGT, SULT, & GST) with ≥ 95% reduction from the average lot values or levels that are statistically not different from background.

i. Human Metabolic Clearance Assay

A human metabolic clearance assay which will measure the rate of hepatic metabolism of a parent compound will be conducted using primary human hepatocytes. Primary human hepatocytes should ideally be a ≥ 10 donor pool from mixed gender adults within the range of 20 to 50 years old. Primary human hepatocytes will be obtained from a documented commercial source, in compliance with any and all federal regulations and shall be similar or equivalent to the source used in Rotroff *et al.* (2010) and Wetmore *et al.* (2012). Other references are available in Appendix B.

ii. Rat Metabolic Clearance Assay

A rat metabolic clearance assay which will measure the rate of hepatic metabolism of a parent compound will be conducted using primary rat hepatocytes. Primary rat hepatocytes should ideally be a > 5 donor pool from mixed gender rats within the range of 8 to 12 weeks old. Primary rat hepatocytes will be obtained from a documented commercial source, in compliance with any and all federal regulations and shall be similar or equivalent to the source used in Wetmore *et al.* (2013). Other references are available in Appendix B.

iii. Rainbow Trout Metabolic Clearance Assay

A rainbow trout metabolic clearance assay which will measure the rate of hepatic metabolism of a parent compound will be developed using primary rainbow trout hepatocytes. Primary rainbow trout hepatocytes should ideally be a > 5 donor pool from mixed gender sexually immature animals. Primary trout hepatocytes will be obtained from a documented source, in compliance with any and all federal regulations. It is expected that the contractor can procure hepatocytes through a commercial source (e.g., https://www.thermofisher.com/us/en/home/industrial/pharma-biopharma/drug-discovery-development/adme-tox/gibco-hepatocytes/trout-hepatocytes.html or https://kjscientific.com/product/cryopreserved-hepatocytes/ or https://www.primacyt.com/primacyt-cryopreserved-hepatocytes/cryo-preserved-animal-hepatocytes/fish-trout-microsomes-subcellular-cytosol-liver/index.php). Special care should be taken to ensure that the trout used are not being treated with hormones. It is recommended that donor animals be sexed and have gonadosomatic index (GSI) measured to evaluate sexual maturity. For this task, along with the citations listed in Appendix B, Fay *et al.* (2015), Fay *et al.* (2014a, b), Nichols *et al.* (2013), Johanning *et al.* (2012) and Han *et al.* (2008) should also be referenced.

C. Analytical Chemistry Methods

i. Gas Chromatography with Mass Spectrometric Detection (GC/MS) Chemical Analysis

This method utilizes a solid phase extraction and equipment should include: autosampler capable of making 2 to 20 µl injections from a 96-well microtiter plate; Waters X-Bridge C18 reversed phase column or equivalent; Micromass Quattro Premier Mass Spectrometer or equivalent. The method has been referenced in Rotroff *et al.* (2010), Wetmore *et al.* (2012) and Wetmore *et al.* (2013). This method will need to be optimized for the specific matrices from the two *in vitro* species-specific assays (i.e., a total of six assays from human plasma to trout hepatocyte) with respect to sample extraction and cleanup.

ii. High Performance Liquid Chromatography with Mass Spectrometric Detection (HPLC/MS) Chemical Analysis

This method utilizes a chromatographic extraction with a C18 column and equipment should include: autosampler capable of making 2 to 20 µl injections from a 96-well microtiter plate; LC binary gradient pump capable of pumping between 0.25 and 2 mL/minute; Waters Alliance 2795 HPLC or equivalent; Micromass Quattro Premier Mass Spectrometer or equivalent. The method has been referenced in Rotroff *et al.* (2010), Wetmore *et al.* (2012) and Wetmore *et al.* (2013). This method will need to be optimized for the specific matrices from the two *in vitro* species-specific assays (i.e., a total of six assays from human plasma to trout hepatocyte) with respect to sample extraction and cleanup.

iii. High (or Ultra-High) Performance Liquid Chromatography with Fluorescence Detection (HPLC/FL or UPLC/FL) Chemical Analysis

This method utilizes an HPLC (UPLC) system equipped with a fluorescence detector, e.g., Waters Acquity UPLC system equipped with a Waters Acquity fluorescence detector (Milford, MA) or equivalent. This method has been referenced in Fay *et al.* (2014 a, b). This method will need to be optimized for the specific matrices from the two *in vitro* species-specific assays (i.e., a total of six assays from human plasma to trout hepatocyte) with respect to sample extraction and cleanup.

D. Deliverables

Within three (3) months of the approval of the QAPP a draft of all the SOPs will be provided to the sponsor for approval. Each SOP should have clearly labeled sections similar to: 1.0 Purpose; 2.0 Scope; 3.0 Responsibilities; 4.0 Procedures; 5.0 References. The draft SOPs will be delivered to the sponsor electronically in MS Word format and all data should be provided in Excel spreadsheets. The sponsor reserves the right to review or modify the SOPs prior to approval. SOPs must be approved before task order work can move forward into proficiency (Task 3.2).

Task 3.2.: Establish Proficiency

****Task 3.2 will be Firm Fixed Price (FFP)

The EPA will provide a list of two (2) proficiency chemicals to be tested in each species-specific assay (three species with two assays per species equals a maximum of 12 proficiency chemicals) and each proficiency chemical must be run on two separate days. It is anticipated that the two chemicals per species-specific assay will be amenable to different analytical chemistry methods listed above, thus providing proficiency for analytical methods concurrent with in vitro methods. Proficiency chemical names will be provided after TO award.

Plasma Protein Binding proficiency runs will test a single concentration and will consist of three replicates sampled at a single time point. Both controls will use a single concentration and will consist of three replicates sampled at the same time point as the test chemical.

Metabolic Clearance proficiency runs will test a single concentration and will consist of three replicates sampled at six time points (e.g., 0, 5, 15, 30, 60, and 90). A negative control will be run concurrently at a single concentration and will consist of two replicates sampled at the same six time points.

For all analytical chemistry methods, proficiency reports must also include information and data on detection limit, sensitivity, instrument precision and accuracy, quantitation limit, linearity, range and robustness.

Within three (3) months of the approval of the SOPs, proficiency reports and data will be provided to the sponsor for approval. The proficiency reports will be delivered to the sponsor electronically in MS Word format and all data should be provided in Excel spreadsheets. Proficiency must be established, via sponsor approval, before task order work can move forward with test chemical analyses (Tasks 3.3 and 3.4).

Task 3.3: Verify/Develop Analytical Chemistry Methods for Test Chemicals
****Task 3.3 will be Time & Materials/Labor Hour (T&M/LH)

After SOPs have been generated and proficiency has been established and verified, EPA will provide chemical lists for testing. *Chemical lists will be provided on a per species basis (e.g., 20 chemicals for human assays and 20 chemicals for rat assays) and likely will have some overlap but will not be identical.* As outlined below under Task 3.4, the EPA will initially request 20 selected chemicals for testing with each species (i.e., human, rat, rainbow trout). For each chemical the most appropriate and best analytical chemistry method must be determined to measure chemical levels from samples generated in the species-specific *in vitro* assays.

The contractor shall be responsible for obtaining chemical stocks and for verifying their purity. Chemical stock purity must be verified to be ≥ 98%. At time of TO award, the minimum order will be met. Optional quantities may be ordered at any time during performance of the TO. The task order will consist of four (4) optional quantities of 20 chemicals for each species.

It is expected that the three (3) analytical chemistry methods in all three (3) species established under Task 3.1 and 3.2 should be adequate for ≥ 95% of the selected test chemicals, however there may need to be other analytical chemistry methods developed. For chemicals requiring an analytical chemistry method different from those outlined under Task 3.1, a workplan and estimated budget must be generated. This workplan/budget will be reviewed and must be approved by the TO COR before efforts to develop an analytical chemistry method are undertaken. For any new analytical methods developed under Task 3.3, SOPs and proficiency runs, as outlined in Tasks 3.1 & 3.2, will be required.

Within four (4) months of the EPA providing lists of test chemicals, the analytical chemistry methods must be finalized to perform the species-specific assays outlined in Task 3.4. For each test chemical, a brief report will be provided to the EPA which outlines the method and clearly indicates the Limit of Quantitation (LOQ) and Level of Detection (LOD) achieved with that method. This report will be in a Word format with all data provided in an Excel format and must be approved by EPA before any in vitro assay testing (Task 3.4.) will occur.

Task 3.4: Perform *In Vitro* Assays with Appropriate Analytical Chemistry Methods
****Task 3.4 will be Firm Fixed Price (FFP)

After analytical chemistry methods have been verified or, where necessary, developed for the selected chemicals, the contractor will perform both species specific *in vitro* assays along with the necessary analytical chemistry analyses for the designated chemicals. ***EPA will request testing with a minimum of 20 discrete chemicals in both in vitro assays listed in Task 3.1 for all three species. There will be four (4) optional quantities/line items for 20 additional chemicals each, for a maximum potential of 100 chemicals for each species.*** Offerors must submit a FFP for the base quantity (i.e., 20 discrete chemicals for each species) and a FFP for each of the four (4) optional quantities (i.e., 20 discrete chemicals for each species). At time of TO award, the minimum order will be funded. Optional quantities may be ordered at any time during performance of the TO.

For each assay definitive run, one (1) reference compound, selected by the sponsor shall be included to demonstrate that the assays are functioning within the expected ranges. The reference chemical chosen for each species and assay will likely be one of the same chemicals used to determine assay proficiency from Task 3.2. Multiple test chemicals can be run concurrently using the same reference chemical, but the test/reference chemical ratio shall not exceed five.

Plasma Protein Binding Assay
Plasma protein binding assays on test chemicals will include a screening run and a definitive run. Controls will be included in each run, but with different parameters.

Screening runs for test chemicals will test two concentrations (e.g., 1 and 10 µM) with two replicates per concentration and will be sampled at two time points (e.g., 4 and 8 hours). Both controls will test only one concentration (generally the higher) and each control will consist of two replicates sampled at the same time points as the test chemicals.

Definitive runs for test chemicals will test a single concentration and will consist of three replicates sampled at a single time point. Both controls will use a single concentration and will consist of three replicates sampled at the same time point as the test chemical.

Metabolic Clearance Assay
Metabolic clearance assays on test chemicals will include screening and definitive runs. Negative controls will be included in each run, but with different parameters. Each run for a given test chemical must have a different concurrent reference chemical run.

Screening runs for test chemicals will test two concentrations (e.g., 0.1 and 1 µM) with two replicates per concentration sampled at four time points (e.g., 0, 15, 60 and 120 min). Negative controls will test one concentration (generally the higher) and will consist of two replicates sampled at two time points (e.g., 0 and 120 min).

Definitive runs for test chemicals will test a single concentration and will consist of one replicate sampled at six time points (e.g., 0, 5, 15, 30, 60, and 90). Each test chemical run must also have a concurrent negative control replicate at the same concentration sampled at the same six time points. Each test chemical must have four independent runs and each of these runs must be done with a separate reference chemical run.

Results from screening runs will be reported to EPA prior to the definitive runs. EPA will assess the data and provide time and concentration guidance on a per chemical-species-assay specific basis through technical directive. Within four (4) months of the EPA approving the analytical method for a test chemical, the relevant in vitro assays screening runs will be completed. For each test chemical, a brief report in Word format will be provided to the sponsor with all data provided in an Excel format.

Task 3.5: Collect, Compile, Review Data and Prepare, Submit Reports
****Task 3.5 will be FFP

When all assays for each test chemical have been completed or at the end of the POP, the contractor shall compile the data into one (1) electronic document. The written report, in MS Word, shall include analytical chemistry results of the stock, methods and results of the *in vitro* assays and analytical chemistry methods, and a section detailing any deviations or observed anomalies. The report must describe the methods and findings and shall include a comparison of test data to any control data with a description of significant findings.

QC shall be conducted on actual calculated numbers and not solely on data recording sheets. If problems are found in 10% of data that initially undergo a random check in accordance with the QC process, the remaining 90% of data shall be reviewed.

The data shall be provided to the TO COR electronically in an MS Excel spreadsheet or other similar electronic format. The data sheets shall be delivered to the TO COR after review by a/the senior scientist for data soundness and scientific relevance. All data shall be submitted (suspected outliers shall not be omitted from the report to EPA). The contractor shall ensure the overall quality of the final reports.

The draft report and data shall be delivered to the TO COR after review by the contractor senior scientist and the contractor Quality Assurance Manager (QAM) for scientific relevance and data soundness, respectively. These deliverables shall be as complete as possible and free of typographical errors and shall be provided as a cohesive unit that encompasses all assays performed for a specific chemical.

Assumptions for Pricing

For Tasks 3.4 and 3.5, offers must include a price per 20 chemicals which includes the analytical chemistry method for: a) both human *in vitro* assays; b) both rat *in vitro* assays; and c) both rainbow trout *in vitro* assays. Optional quantities will be stated as optional line items in the TO award and may only be ordered via modifications to the TO by the Contracting Officer. The minimum quantity (i.e., 20 chemicals for both assays in each species) is guaranteed and will be funded at the time of TO award.

Reference List

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Rotroff DM, BA Wetmore, DJ Dix, SS Ferguson, HJ Clewell, KA Houck, EL LeCluyse, ME Andersen, RS Judson, CM Smith, MA Sochaski, RJ Kavlock, F Boellmann, MT Martin, DM Reif, JF Wambaugh, RS Thomas. 2010. Incorporating human dosimetry and exposure into high- throughput *in vitro* toxicity screening. Toxicol Sci. 117:348-358.

Wetmore BA, JF Wambaugh, SS Ferguson, MA Sochaski, DM Rotroff, K Freeman, HJ Clewell III, DJ Dix, ME Andersen, KA Houck, B Allen, RS Judson, R Singh, RJ Kavlock, AM Richard, RS Thomas. 2012. Integration of dosimetry, exposure, and high-throughput screening data in chemical toxicity assessment. Toxicol Sci. 125: 157-174.

Wetmore BA, JF Wambaugh, SS Ferguson, L Li, HJ Clewell III, RS Judson, K Freeman, W Bao, MA Sochaski, T Chu, MB Black, E Healy, B Allen, ME Andersen, RD Wolfinger and RS Thomas. 2013. Relative impact of incorporating pharmacokinetics on predicting *in vivo* hazard and mode of action from high-throughput *in vitro* toxicity assays. Toxicol Sci. 132: 327-346.

Wetmore BA. 2014. Quantitative *in vitro*-to-*in vivo* extrapolation in a high-throughput environment. Toxicol Sci. Epub. doi: 10.1016/j.tox.2014.05.012

Wetmore BA, B Allen, HJ Clewell III, T Parker, JF Wambaugh, LM Almond, MA Sochaski and RS Thomas. 2014. Incorporating Population Variability and Susceptible Subpopulations into Dosimetry for High-Throughput Toxicity Testing. Toxicol Sci. Epub. Doi: 10.1093/toxsci/kfu169.

APPENDIX A

Other potential references which inform on this procedure are listed below:

Nigel J Waters, Rachel Jones, Gareth Williams, and Bindi Sohal, "Validation of a Rapid Equilibrium Dialysis approach for the measurement of plasma protein binding," J. Pharm. Sci. 97(10): 4586-4595 (2008).

Mark G. Qian, Tai-Nang Huang, Susan Chen, Ji Zhang, Cindi Xia, Chuang Lu, Jin-Tao Wu, and Frank W. Lee, Millennium Pharmaceuticals, Poster: "High throughput plasma protein binding assay using rapid equilibrium dialysis (RED™) Device," http://www.piercenet.com/files/ISSX_poster_mqian_20071001.pdf.

Michael J. Banker, Tracey H. Clark, and John A. Williams, "Development and validation of a 96-well equilibrium dialysis apparatus for measuring plasma protein binding," J. Pharm. Sci. 92(5): 967-974 (2003).

Ilona Kariv, Hong Cao, and Kevin R. Oldenberg, "Development of a high throughput equilibrium dialysis method," J. Pharm. Sci. 90(5): 580-587 (2001).

Christopher J. Kochansky, Daniel R. McMasters, Ping Lu, Kenneth A, Koeplinger, Haley H. Kerr, Magang Shou, and Kenneth R. Korzekwa, "Impact of pH on plasma binding in equilibrium dialysis," Molecular Pharmaceutics 5(3): 438-448 (2008).

APPENDIX B

Other potential references for this procedure are listed below:

Ito K and Houston JB (2004) Comparison of the use of liver models for predicting drug clearance using in vitro kinetic data from hepatic microsomes and isolated hepatocytes. Pharm. Res. 21:785-792.

Lave T *et al.*, (1997) The use of human hepatocytes to select compounds based on the expected hepatic extraction ratios in humans. Pharm. Res. 14:152-155.

Obach RS *et al.*, (1997) The prediction of human pharmacokinetic parameters from preclinical and in vitro metabolism data. J. Pharmacol. Exp. Therap. 283:46-58.

Mark G. Qian, Tai-Nang Huang, Susan Chen, Ji Zhang, Cindi Xia, Chuang Lu, Jin-Tao Wu, and Frank W. Lee, Millennium Pharmaceuticals, Poster: "High throughput plasma protein binding assay using rapid equilibrium dialysis (RED™) Device," http://www.piercenet.com/files/ISSX_poster_mqian_20071001.pdf.

Michael J. Banker, Tracey H. Clark, and John A. Williams, "Development and validation of a 96-well equilibrium dialysis apparatus for measuring plasma protein binding," J. Pharm. Sci. 92(5): 967-974 (2003).

Ilona Kariv, Hong Cao, and Kevin R. Oldenberg, "Development of a high throughput equilibrium dialysis method," J. Pharm. Sci. 90(5): 580-587 (2001).

Christopher J. Kochansky, Daniel R. McMasters, Ping Lu, Kenneth A, Koeplinger, Haley H. Kerr, Magang Shou, and Kenneth R. Korzekwa, "Impact of pH on plasma binding in equilibrium dialysis," Molecular Pharmaceutics 5(3): 438-448 (2008).

1.6 TASK 4 OPTIONAL: TESTS TO DETERMINE PHYSICAL CHEMICAL PROPERTIES OF SELECT CHEMICALS

Purpose: The purpose of Task 4 is to fill in data gaps to better understand physical-chemical domains of applicability for HT testing. One of the key considerations associated with utilizing high throughput (HT) screening data as an alternative to low throughput (LT) screening data for EDSP Tier 1 assays are limitations based on physical-chemical properties. One particular physical-chemical limitation is potential volatilization of the test article, especially for long duration assays or open systems. This process is exacerbated by substances that volatilize more readily. To have confidence in the results, regulators must be certain that the test article has remained in the test system throughout the duration of the assay. There are other physical-chemical processes that can affect the outcome of an assay - including solubility, potential to adhere to the well walls, and reactivity with the test platform– that may or may not impact the biological processes of delivery to or effect of an xenogenous substance on a site of a potential toxicity. Physical-chemical properties affect many different types of testing, including in vivo, in vitro, and reverse toxicokinetic assays. While physical-chemical property testing may exist for many substances, many results are often of limited quality (or the study quality results were never evaluated in the first place). Where testing does not exist, models can often fill the gap, but these are also of varying quality. As such, there is often a need to fill in data gaps in order to better understand physical-chemical domains of applicability for HT testing.

For this task, EPA shall provide available data and work completed to date. Contractor may propose additional approaches and data sources for EPA consideration. Any code or scripts (including statistical analysis) developed and data gathered shall be made available to EPA for eventual public release. Unless proposed and accepted by EPA, Contractor shall develop all code and scripts (including statistical analysis) in Python 3 or R 3.4 or higher. Unless proposed and accepted by EPA, Contractor shall utilize open-source or freely available toolkits and libraries. The Contractor shall maintain and provide any code developed for this project in a versioning repository such as Git or BitBucket.

Task 4.1.: Physical-Chemical Property Testing

****Task 4.1 will be Firm Fixed Price (FFP)

By technical directive, the Contractor shall obtain, store, and test a single substance according to one or more of the following EPA or OECD physical-chemical property guidelines (Table 1).

Table 1

EPA TG	EPA TG Name	OECD Equivalent	Date Published
830.7000	pH	122	August 1996
830.7050	UV/Visible Absorption	101	August 1996
830.7100	Viscosity	114	August 1996
830.7200	Melting Point/Melting Range	102	March 1998
830.7220	Boiling Point/Boiling Range	103	August 1996
830.7300	Density/Relative Density/Bulk Density	109	June 2002
830.7370	Dissociation Constants in Water	112	August 1996
830.7550	Partition Coefficient (n-octanol/water), Shake Flask Method	107	August 1996
830.7560	Partition Coefficient (n-octanol/water), Generator Column Method	none	August 1996
830.7570	Partition Coefficient (n-octanol/water), Estimation by Liquid Chromatography	117	August 1996
830.7840	Water Solubility: Column Elution Method; Shake Flask Method	105	March 1998
830.7860	Water Solubility, Generator Column Method	none	March 1998
830.7950	Vapor Pressure	104	August 1996
835.2120	Hydrolysis [SUPERSEDES 835.2110]	111	November 2008
835.2130	Hydrolysis as a Function of pH and Temperature	none	January 1998
835.2210	Direct Photolysis Rate in Water by Sunlight	none	January 1998
835.2240	Photodegradation in Water	none	November 2008

Cost assumptions:
Provide firm-fixed pricing for a single chemical on a per test basis.
Assume each chemical substance shall cost $100/sample to obtain.

As noted in each test guideline, the test guidelines are not, in an of themselves, testing protocols. The contractor will need to develop appropriate testing protocols (including, where appropriate, analytical verification techniques) and submit these to EPA for review.

Task 4.2.: Physical-Chemical Domains of Applicability for HT Testing

****Task 4.2 will be Time & Materials/Labor Hour (T&M/LH)

By technical directive, the contractor shall, in conjunction with EPA, optionally design and implement a suitable test protocol and chemical-analytical verification system to detect the presence and/or fate of chemical substances in model high-throughput test platforms.

Cost assumptions:

- Assume the cost estimate is for a single chemical and optional quantities are for a single chemical. Assume that EPA may order more than one chemical at a time, e.g., quantity of 5 to 10 chemicals at a time. EPA will specify the number of chemicals via technical directive.
- Assume that EPA shall test chemical substances in the following custom experimental design, but using metabolically inactivated (dead) cells:
- ToxCast ACEA_ER_80hr Assay Protocol
- (protocols available at https://www.epa.gov/chemical-research/toxcast-data-generation-toxcast-assays).
- Analytical methods that can detect ppb levels of test substances will be selected or developed for the study. A suitable and validated analytical method will be used to measure concentration of the test article versus time. Triplicate wells will be subjected to quantitative chemical analysis for the test substance at the following time points (0, 1, 2, 4, 8, 16, 32, and 80 hours) of the assay.
- Metabolically inactivated cells will be prepared using appropriate methods (e.g., multiple rigorous freeze/thaw cycles). These will be prepared as in advance, aliquoted and stored frozen until needed.
- Assume the chemical substance shall cost $100/sample to obtain and has already been tested in the ToxCast assay above.

1.7 REPORTING REQUIREMENTS AND DELIVERABLES

The contractor shall provide the following deliverables listed in Table 2.

Table 2 Deliverables and Schedule

Tasks	Deliverables	Due Dates
Task 1	Task management ✓ Kick-off meeting within 2 weeks after the task order has been awarded. ✓ Monthly Progress Report (i.e. Technical/Progress Status Report and Financial Status Report) by the 15th of each month (following completion of 1st reporting period). ✓ Biweekly status meetings ✓ Other meetings as required by the TOCOR ✓ Email a copy to the CO, Contract level COR, TOCOR, and Alt TOCOR ✓ Immediately inform the TOCOR when any hours or costs for any task has exceeded or is expected to exceed the contractor estimate by >10%. ✓ Immediately inform the TOCOR of any problems that may impact the production, budget, and/or delivery of deliverables. ✓ The Contractor shall notify the TOCOR when 75% of the Government approved hours or approved LH costs have been incurred (including unbilled hours and costs).	
Task 2	EPA Requirements for Quality Assurance Project Plans (QA/R- 5) https://www.epa.gov/quality/epa-qar-5-epa-requirements-quality-assurance-project-plans ✓ Draft QAPP ✓ Final QAPP	✓ Draft QAPP. Within 10 business days after Task Order Award. ✓ Final QAPP. Within 5 business days of receipt of the written comments on the draft QAPP, unless otherwise instructed by the EPA TO COR.

Tasks	Deliverables	Due Dates
Task 3.1	✓ Draft SOPs will be provided to the sponsor for approval. Each SOP should have clearly labeled sections similar to: 1.0 Purpose; 2.0 Scope; 3.0 Responsibilities; 4.0 Procedures; 5.0 References. The draft SOPs will be delivered to the sponsor electronically in MS Word format and all data should be provided in Excel spreadsheets.	Within three (3) months of the approval of the QAPP generated under Task 2.
Task 3.2	Proficiency reports and data will be provided to the sponsor for approval. The proficiency reports will be delivered to the sponsor electronically in MS Word format and all data should be provided in Excel spreadsheets	Within three (3) months of the approval of the SOPs generated under Task 3.1.
Task 3.3	The analytical chemistry methods must be finalized to perform the species-specific assays outlined in Task 3.4. For each test chemical, a brief report will be provided to the EPA which outlines the method and clearly indicates the Limit of Quantitation (LOQ) and Level of Detection (LOD) achieved with that method. This report will be in a Word format with all data provided in an Excel format	Within four (4) months of the EPA providing lists of test chemicals via technical directive.
Task 3.4	Results from screening runs will be reported to EPA prior to the definitive runs. EPA will assess the data and provide time and concentration guidance on a per chemical-species-assay specific basis through technical directive. For each test chemical, a brief report in Word format will be provided to the sponsor with all data provided in an Excel format.	Within four (4) months of the EPA approving the analytical method for a test chemical (under Task 3.3).
Task 3.5	When all assays for each test chemical have been completed or at the end of the POP, the contractor shall compile the data into one (1) electronic document. The written report, in MS Word, shall include analytical chemistry results of the stock, methods and results of the *in vitro* assays and analytical chemistry methods, and a section detailing any deviations or observed anomalies. The report must describe the methods and findings and shall include a comparison of test data to any control data with a description of significant findings.	Within three (3) months of completing generation of all data under Task 3.4.

Tasks	Deliverables	Due Dates
Task 4.1	Physical-Chemical Properties Testing results	TBD by technical directive
Task 4.2	Physical-Chemical Domains of Applicability for HT Testing results	TBD by technical directive

1.8 ACCEPTABLE QUALITY LEVEL FOR TASKS

See Attachment 1: Quality Assurance Surveillance Plan

1.9 PERIOD OF PERFORMANCE

The period of performance of this task order is:

BASE POP: 36 months from award date

CLIN 1: Base Task 1-3 [Non-severable work]
CLIN 2: Task 3 Optional Quantities [Non-severable work]
CLIN 3: Optional Task 4 [Severable work]

1.10 PLACE OF PERFORMANCE

Work may be performed off-site.

1.11 PERSONNEL

The Contractor is responsible for providing personnel with the necessary level expertise to support the task activities and requirement in this PWS.

1.12 TASK ORDER TYPE: TIME & MATERIALS OR FIRM FIXED PRICE

1.13 GOVERNMENT FURNISHED EQUIPMENT (GFP)

In accordance with FAR 45.102, the contractor shall furnish all property required for performing Government contracts. If a contractor believes that Government property is required for performance of the contract, the contractor shall submit a written request to the CO. For cost purposes, assume that EPA shall provide an office phone with voicemail, and e-mail for approved personnel working in OSCP-space to complete work under Task 3 of this task order.

1.14 TRAVEL

The Contractor may be required to travel in the course of the performance of this task order. The Contractor is required to follow the requirements of subpart 31.2 of the FAR regulations in incurring allowable travel costs under this task order, and correspondingly must at all times seek and obtain government rates whenever available and observe current subsistence ceilings.

1.15 TRAINING

EPA-H-31-105 APPROVAL OF TRAINING [see Section H.22 of the IDIQ contract]

(a) The contractor shall provide and maintain a qualified staff of personnel to meet the requirements of the Performance Work Statement. The contractor shall provide training to keep its personnel abreast of changes to the science and/or technology associated with the requirements of the contract. In addition, the contractor shall ensure that its personnel receive appropriate safety, health and environmental training in accordance with Federal, state and local requirements prior to assigning any task that require such training. The contractor shall provide documentation of such training upon the request of the Contract-Level COR and/or Contracting Officer.

The Government will not directly reimburse the cost for contractor employees to meet or maintain minimal contract requirements or to obtain and sustain an appropriate level of professionalism. Any direct charges for training will only be considered for reimbursement under this contract by compliance with the procedures set forth in paragraph (b) (see Section H.22 of the IDIQ contract).

2 INSPECTION AND ACCEPTANCE

QUALITY ASSURANCE PROJECT PLAN (SEE TASK 2 ABOVE)

The Contractor shall submit a draft QAPP per EPA Requirements for Quality Assurance Project Plans (QA/R-5) (Table 3).

Table 3. Quality Assurance Project Plan

	Documentation	Specifications	Due
X	Quality Assurance Project Plan for the Task Order	EPA Requirements for Quality Assurance Project Plans (QA/R-5) (dated 3//20/2011) https://www.epa.gov/quality/epa-qar-5-epa-requirements-quality-assurance-project-plans	✓ Draft QAPP. Within 10 business days after Task Order Award. ✓ Final QAPP. Within 5 business days of receipt of the written comments on the draft QAPP, unless otherwise instructed by the EPA TO COR.

3 TASK ORDER ADMINISTRATION DATA

3.1 CONTRACT ADMINISTRATION REPRESENTATIVES

- Contracting Officer: Jody Gosnell, Team Leader OAS/HQAD
- Contract Specialist: Eric Ward, OAS/HQAD
- Contract Level Contracting Officer's Representative: Sharlene Matten, OSCP/EACPD

- Task Order Contracting Officer's Representative: Scott Lynn, OSCP/EACPD

3.2 TASK ORDER CLAUSES

INVOICING

Invoices shall be submitted in accordance with contract clause G.3 EPAAR 1552.232-70 SUBMISSION OF INVOICES. (JUN 1996) - ALTERNATE I (JUN 1996).

3.3 EPA-J-52-101 LIST OF ATTACHMENTS

Attachment 1: QUALITY ASSURANCE SURVEILLANCE PLAN

3.4 INSTRUCTIONS, CONDITIONS, AND NOTICES TO OFFERORS

EPA-L-36-101 RFTOP PROPOSAL INSTRUCTIONS

The offeror's response shall not exceed 15 double sided pages each and shall include all charts, illustrations, etc. This limitation does not include resumes. Font size: must be 11 points or larger (smaller text in figures, graphs, diagrams and charts is acceptable as long as it is legible when the page is viewed at 100%).

(a) TECHNICAL PROPOSAL INSTRUCTIONS:

(1) The technical proposal shall be complete and demonstrate an understanding of the work to be provided and the contractor's ability to perform the work in accordance with PWS. The technical proposal shall address all of the technical evaluation criteria presented in this section.

(2) Each section of the proposal shall be titled.

(3) Subcontractors

Each offeror shall list in a table format the name and addresses of all subcontractors who will perform work or labor or render services to the offeror for compensation in an amount in excess of one percent of the offeror's total price. Each offeror shall show on the table the portion of the work to be done by each subcontractor. This table shall be included with the technical proposal. The table shall include: (a) the name and address of the subcontractor, (b) a short description of the work the subcontractor will be designated to perform or deliver, (c) the portion in percent of the work (LOE) the subcontractor will be designated to perform or deliver.

(4) Conflict of Interest

- Vendors shall provide a completed version of the certification at EPA-H-09-106 task order conflict of interest certification as part of its Technical Proposal. The complete certification will not count against the page limitations for the Technical Proposal.
- Consistent with the terms of the prime contract, vendors shall disclose any actual or potential conflict of interest to the Contracting Officer within 7 days after receipt of the Request for Task Order Proposal. The disclosure shall include a description of actions which the Contractor has taken or proposes to take, after consultation with the Contracting Officer, to avoid, mitigate, or neutralize the actual or potential conflict of interest.

(b) TECHNICAL EVALUATION CRITERIA

Technical Evaluation Factors listed below are of equal importance.

Factor 1 – Technical Approach: The Contractor shall propose their Technical Approach for accomplishing the objectives, requirements, and tasks and subtasks of the task order.

Factor 2 – Staffing Approach: The Contractor shall describe their staffing approach in the form of a Staffing Plan. The Plan shall describe the role and level of involvement of each proposed team member in implementing the required tasks.

(c) COST PROPOSAL

Instructions:

The purpose of these cost instructions is to assist offerors in submitting information required to evaluate the reasonableness of proposed costs. All dollar amounts provided shall be rounded to the nearest dollar. The labor rates used for this task order shall not exceed the labor rates included in the base IDIQ contract. However, EPA will accept discounted rates.

Travel costs shall not exceed $2,500 (BASE plus all Option Years). Contractors are encouraged to use public transportation.

ATTACHMENT 1

QUALITY ASSURANCE SURVEILLANCE PLAN

QUALITY ASSURANCE SURVEILLANCE PLAN

PERFORMANCE REQUIREMENT	PERFORMANCE MEASURE (PM)	PERFORMANCE STANDARD	SURVEILLANCE METHOD	INCENTIVES & DISINCENTIVES
MANAGEMENT AND COMMUNICATION: The contractor shall maintain contact with the EPA CO, COR, and TOCOR throughout the performance of the contract.	Contractor shall immediately bring potential problems to the appropriate EPA personnel and shall recommend actions that would mitigate or resolve the problem.	Issues that impact project schedules and costs shall be brought to the attention of the EPA within 3-days of occurrence.	All active task orders will be reviewed by the EPA to identify unreported issues.	Performance will be considered in the award of subsequent task orders and will be factored into the annual evaluation of Business Relations in the Contractor Performance Assessment Reporting System (CPARS).
TIMELINESS: For every Task Order awarded establishing a firm, specific delivery date for the generation of a report, the contractor shall deliver such report to the COR, TOCOR and CO no later than the time specified in the order's PWS.	Deliverables and related work must comply with contractual timeliness requirements. The contractor will be evaluated on its responsiveness to all task orders.	95% of all deliverables and related work shall be completed on time within task schedule and/or tech. direction requirements.	100% inspection of all deliverables and related work by the TOCOR; TOCOR will document the timeliness of all work requirements.	Performance will be considered in the award of subsequent task orders and will be factored into the annual evaluation of Timeliness in the Contractor Performance Assessment Reporting System (CPARS).
TECHNICAL QUALITY: For every task order awarded, the analyses conducted by the contractor shall be factual, defensible, credible, and based on sound scientific methods. All data shall be collected from reputable sources and quality assurance measures shall be conducted in accordance with the agency requirements outlined in the task orders.	All deliverables and related work must be complete, accurate, thorough, and professionally credible.	Data are 100% accurate; review demonstrates a high level of expertise and credibility with regard to personnel and use of scientific methodology. Task Orders shall be conducted in strict conformance with approved QA plans. Outputs shall withstand internal review by the US EPA and outside scientific reviewers.	EPA Staff will conduct secondary reviews of work completed by the contractor. Feedback will be provided.	Performance will be considered in the award of subsequent task orders and will be factored into the annual evaluation in the category of Quality of Product or Service in the Contractor Performance Assessment Reporting System (CPARS).

TASK ORDER CLAUSES

Period of Performance

The period of performance of this task order is 09/19/2019 – 09/18/2022

Submission of Invoices

Invoices shall be submitted in accordance with EPAAR 1552.232-70 SUBMISSION OF INVOICES. (JUN 1996) - ALTERNATE I (JUN 1996). See address below.

RTP Finance Center

US Environmental Protection Agency

RTP-Finance Center (AA216-01)

109 TW Alexander Drive

www2.epa.gov/financial/contracts

Durham NC 27711

E.2 Period of Performance

Base: 36 months from award date

F. TASK ORDER TYPE

Time and Materials & Firm Fixed Price

G. INSPECTION AND ACCEPTANCE

G.1 Quality Assurance Project Plan

The contractor shall submit the following quality system documentation to the CO at the time frames identified below:

Documentation	Specifications	Due
Quality Assurance Project Plan for the Task Order	EPA Requirements for Quality Assurance Project Plans (QA/R-5) [dated03/20/11]	Task Order proposal due date

This documentation can be found on the following EPA website –

https://www.epa.gov/quality/epa-qar-5-epa-requirements-quality-assurance-project-plans

This documentation will be prepared in accordance with the specifications identified above or equivalent specifications defined by EPA.

The Government will review and return the quality documentation, with comments, and indicating approval or disapproval. If necessary, the contractor shall revise the documentation to address all comments and shall submit the revised documentation to the government for approval.

The contractor shall not commence work involving environmental data generation or use until the Government has approved the quality documentation.

H. TASK ORDER ADMINISTRATION DATA

H.1 Contract Administration Representatives

Contracting Officer: Jody Gosnell, Gosnell.jody@epa.gov

Contracting Officer's Representative: Sharlene Matten, matten.sharlene@epa.gov

I. INVOICING

Invoices shall be submitted in accordance with contract clause G.3 EPAAR 1552.232-70 SUBMISSION OF INVOICES. (JUN 1996) - ALTERNATE I (JUN 1996).

J. TASK ORDER CLAUSES

Local Clauses EPA-H-42-102 UTILIZATION OF FEDCONNECT FOR CONTRACT ADMINISTRATION

EPA will utilize the FedConnect® web portal in administering this contract. The contractor must be registered in FedConnect® and have access to the FedConnect website located at https://www.fedconnect.net/Fedconnect/. For assistance in registering or for other FedConnect® technical questions please call the FedConnect® Help Desk at (800) 899-6665 or email at support@fedconnect.net.

FAR 52.216-18 ORDERING. (OCT 1995)

(a) Any supplies and services to be furnished under this contract shall be ordered by issuance of delivery orders or task orders by the individuals or activities designated in the Schedule. Such orders may be issued from **09/19/2019** through **09/18/2022**.

(b) All delivery orders or task orders are subject to the terms and conditions of this contract. In the event of conflict between a delivery order or task order and this contract, the contract shall control.

(c) If mailed, a delivery order or task order is considered "issued" when the Government deposits the order in the mail. Orders may be issued orally, by facsimile, or by electronic commerce methods only if authorized in the Schedule.

FAR 52.216-19 ORDER LIMITATIONS. (OCT 1995)

(a) *Minimum order*. When the Government requires supplies or services covered by this contract in an amount of less than $10,000.00, the Government is not obligated to purchase, nor is the Contractor obligated to furnish, those supplies or services under the contract.

(b) *Maximum order*. The Contractor is not obligated to honor-

(1) Any order for a single item in excess of $4.5 Million;

(2) Any order for a combination of items in excess of $4.5 Million; or

(3) A series of orders from the same ordering office within 7 days that together call for quantities exceeding the limitation in subparagraph (b)(1) or (2) above.

(c) If this is a requirements contract (*i.e.*, includes the Requirements clause at subsection 52.216-21 of the Federal Acquisition Regulation (FAR)), the Government is not required to order a part of any one requirement from the Contractor if that requirement exceeds the maximum-order limitations in paragraph (b) above.

(d) Notwithstanding paragraphs (b) and (c) above, the Contractor shall honor any order exceeding the maximum order limitations in paragraph (b), unless that order (or orders) is returned to the ordering office within 3 days after issuance, with written notice stating the Contractor's intent not to ship the item (or items) called for and the reasons. Upon receiving this notice, the Government may acquire the supplies or services from another source.

FAR 52.217-8 OPTION TO EXTEND SERVICES. (NOV 1999)

The Government may require continued performance of any services within the limits and at the rates specified in the contract. These rates may be adjusted only as a result of revisions to prevailing labor rates provided by the Secretary of Labor. The option provision may be exercised more than once, but the total extension of performance hereunder shall not exceed 6 months. The Contracting Officer may exercise the option by written notice to the Contractor within 30 days before the contract expires.

FAR 52.217-9 OPTION TO EXTEND THE TERM OF THE CONTRACT (MAR 2000)

(a) The Government may extend the term of this contract by written notice to the Contractor within 30 days; provided that the Government gives the Contractor a preliminary written notice of its intent to extend at least 60 days before the contract expires. The preliminary notice does not commit the Government to an extension.

(b) If the Government exercises this option, the extended contract shall be considered to include this option clause.

(c) The total duration of this contract, including the exercise of any options under this clause, shall not exceed 36 months.

FAR 52.252-2 CLAUSES INCORPORATED BY REFERENCE. (FEB 1998)

This contract incorporates one or more clauses by reference, with the same force and effect as if they were given in full text. The full text of a clause may be accessed electronically at this/these address(es): FAR: http://farsite.hill.af.mil/vmfara.htm ; EPAAR: http://farsite.hill.af.mil/vmepaara.htm

FAR 52.217-7 -- Option for Increased Quantity -- Separately Priced Line Item.

As prescribed in 17.208(e), insert a clause substantially the same as the following:

Option for Increased Quantity -- Separately Priced Line Item (Mar 1989)

The Government may require the delivery of the numbered line item, identified in the Schedule as an option item, in the quantity and at the price stated in the Schedule. The Contracting Officer may exercise the option by written notice to the Contractor within ***10 days***. Delivery of added items shall continue at the same rate that like items are called for under the contract, unless the parties otherwise agree.